The alkylthiol molecule adsorbs strongly through the sulfur (SH) head group to the substrate surface to form densely packed monolayer films with fully extended hydrocarbon [—$(CH_2)_n$ —] chains, as shown in FIG. **2**. It is believed that upon chemisorption on the substrate, the thiol head group loses its hydrogen to form a thiolate. Because the alkylthiolate molecules are anchored to the gold or silver by the sulfur head, the exposed surface of the monolayer is comprised of the terminal functional group R. By varying the identity of the R group, the surface properties of the SAMs can be tailored for a particular application.

FIGS. **3***a* through **3***c* illustrate the structure of the substrate and SAM as the respective steps of the process according to the invention are performed. In FIG. **3***a*, a mask element **30** is placed over the SAM **31**, and ultraviolet light **32** is radiated onto the surface of the SAM through openings in the mask, which are arranged in a desired pattern, while the SAM is also exposed to air, oxygen, nitrous oxide, or other oxidizing gases. As shown in FIG. **3***b*, in the exposed portions of the SAM, irradiation with ultraviolet light in air causes the alkylthiolate to be oxidized to the corresponding alkylsulfonate, which is weakly bound to the substrate surface. Following irradiation, the substrate is immersed in a solution of a different alkylthiol, and the weakly bound alkylsulfonates are displaced and exchanged for the second alkylthiol molecules in the desired pattern, as shown in FIG. **3***c*. In the unexposed areas, the first alkylthiolate is retained.

FIG. **4** is a schematic representation of an alternative arrangement in which the surface of a SAM on a substrate is exposed to a pattern of light by means of appropriate optics, such as a projection lithography configuration. UV light **40** from a UV light source **41** is directed through a mask **42** having a desired pattern of opaque portions **43** and light transparent portions **44** to form a corresponding UV light exposure pattern or image **45**. Light image **45** is then directed through an optical system **46** to produce a focused image **47**. The optical system **46** directs image **47** onto a SAM **48** formed on a substrate **49** in air, whereby the thiolate head groups in the exposed areas of the monolayer are oxidized to sulfonate groups. The molecules in the exposed areas can then be exchanged for other thiolate molecules as described above.

By judicious choice of the alkylthiol molecules, the process according to the invention can be used to define regions on a surface that will strongly promote and retard the adsorption of selected biological molecules. Thus, the pattern monolayer acts as a molecular template to direct the adsorption of biomolecules on the surface.

For example, the foregoing technique can be used to deposit a protein on a molecular surface in accordance with a predetermined micropattern. Using the techniques of ellipsometry and contact angle wetting, it was established that a protein adsorbs strongly to carboxylic acid-terminated thiol monolayers and very little to perfluorinated thiol monolayers. Thus, by creating a pattern of carboxylic acid monolayer in a perfluorinated monolayer (or vice versa), and then immersing the sample in a protein solution, the protein can be made to "stick" on the parts of the surface that contain only the carboxylic acid groups.

The surfaces of the thiolate SAMs can be designed to effect either specific or nonspecific binding of biological molecules. Specific binding is a strong and specific interaction without covalent bonding between two species such as proteins-receptors, enzymes-substrates, antibodies-antigens and DNA-oligonucleotide probes. Specific binding involves molecular recognition or "handshaking" and may be thought of in terms of a lock and key model where a molecule fits snugly into a quasi-depression or molecular pocket of its binding partner. Numerous interactions between different functional groups may account for the coupling. One example of specific binding is biotin-avidin coupling. Avidin, a large protein, has four separate binding cavities that will each accommodate one biotin molecule. The binding of biotin by avidin is very strong and highly specific. Another well known example of specific binding is the zipping together of one strand of DNA with another or hybridization of a DNA strand with a complementary oligonucleotide probe.

Specific binding can be used to selectively attach DNA probes to SAM surfaces which have been UV-photopatterned. The patterning of large arrays of different DNA probes on a microchip surface is useful in applications involving DNA sequencing or clinical diagnosis of genetic or infectious diseases. The patterned arrays of probes are exposed to an unknown sample of DNA to be analyzed, and the chip can then detect and readout which if any of the probes in the patterned array has bound the unknown DNA sample. From this information it is possible to derive useful information about the sequence of the unknown DNA or in diagnostic applications to verify the presence of DNA sequences which are characteristic of genetic diseases or indicative of the presence of DNA of viruses or bacteria.

Nonspecific binding can be very strong but normally lacks the shape selectivity and multiple interactions of different functional groups associated with specific binding. An example of nonspecific binding is the adsorption of avidin on carboxylic-acid terminated SAMs. The interaction in such a case is believed to be primarily electrostatic. The avidin molecule has a net positive charge, while the carboxy-terminated SAM has a net negative charge, so that the two will attract each other. The binding is nonspecific because any protein or other molecule possessing a net positive charge will bind to the SAM surface.

The steps performed in depositing a protein pattern, as described above, are illustrated in FIGS. **5***a*–**5***c*. In FIG. **5***a*, a SAM of perfluorinated thiol **1** is formed on a gold surface. The perfluorinated SAM is then irradiated with photopatterned ultraviolet light, as shown in FIG. **5***b*, and the UV exposed perfluorinated SAM is immersed in a solution of carboxylic acid-terminated thiol **2**. Thiol **2** adsorbs in the regions that were exposed to the UV light, as shown in FIG. **5***c*. In the unexposed areas perfluorinated thiol **1** is retained, and a patterned SAM is thus produced, comprised of thiol **1** and thiol **2**. Finally, as shown in FIG. **5***d*, the patterned SAM is immersed in a solution of protein, which adsorbs only to the regions of the surface containing the carboxylic acid-terminated thiol **2**, resulting in the patterning of the protein surface.

The foregoing general strategy of manipulating the chemical reactivity of surfaces via the photopatterning process to direct the placement of biomolecules on surfaces may be applicable to a wide variety of biological molecules and/or cells. In addition, the same process may be used to pattern multiple biological species by repeating the second through the fourth steps. A schematic of such a system is shown in FIG. **6**. The ability to fabricate arrays of different biological species on surfaces with micron resolution has important technological potential for biosensing and diagnostic procedures. The advantages of such biosensing arrays in diagnostics include low cost, small size, and most importantly, the ability to perform hundreds of diagnostic tests on a single small test sample.

Finally, it is noted that the patterned monolayers according to the invention can also act as resists for the selective